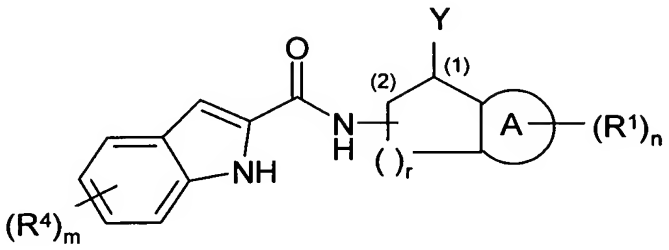
In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claims

1. (original) A compound of formula (1):



(1)

wherein:

A is phenylene or heteroarylene;

n is 0, 1 or 2;

m is 0, 1 or 2;

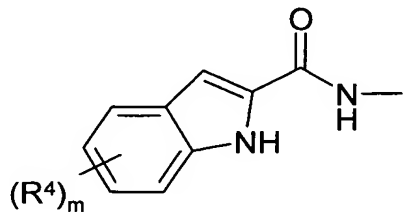
R^1 is independently selected from halo, nitro, cyano, hydroxy, carboxy, carbamoyl, *N*-(1-4C)alkylcarbamoyl, *N*,*N*-((1-4C)alkyl)$_2$carbamoyl, sulphamoyl, *N*-(1-4C)alkylsulphamoyl, *N*,*N*-((1-4C)alkyl)$_2$sulphamoyl, -S(O)$_b$(1-4C)alkyl (wherein b is 0,1,or 2), -OS(O)$_2$(1-4C)alkyl, (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy, (1-4C)alkanoyl, (1-4C)alkanoyloxy, hydroxy(1-4C)alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy and -NHSO$_2$(1-4C)alkyl;

or, when n is 2, the two R^1 groups, together with the carbon atoms of A to which they are attached, may form a 4 to 7 membered saturated ring, optionally containing 1 or 2 heteroatoms independently selected from O, S and N, and optionally being substituted by one or two methyl groups;

R^4 is independently selected from halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy and (1-4C)alkanoyl;

r is 1 or 2; and

when r is 1 the group



is a substituent on carbon (2) and

when r is 2 (thereby forming a six membered ring) the same group is a substituent on carbon (2) or on carbon (3);

Y is selected from $-C(O)R^2$, $-C(O)OR^2$, $-C(O)NR^2R^3$, -(1-4C)alkyl [optionally substituted by 1 or 2 substituents independently selected from hydroxy, $-C=NR^2$, (1-4C)alkoxy, aryloxy, heterocyclyloxy, $-S(O)_bR^2$ (wherein b is 0, 1 or 2), $-O-S(O)_bR^2$ (wherein b is 0, 1 or 2), $-NR^2R^3$, $-N(OH)R^2$, $-NR^2C(=O)R^2$, $-NHOHC(=O)R^2$, $-SO_2NR^2R^3$, $-N(R^2)SO_2R^2$, aryl and heterocyclyl], -C(O)NOH, -C(O)NSH, -C(N)OH, -C(N)SH, $-SO_2H$, $-SO_3H$, $-SO_2N(OH)R^2$, -(2-4C)alkenyl, $-SO_2NR^2R^3$, -(1-4C)alkylC(O)R^2, -(1-4C)alkylC(O)OR^2, -(1-4C)alkylSC(O)R^2, -(1-4C)alkylOC(O)R^2, -(1-4C)alkylC(O)NR^2R^3, -(1-4C)alkylOC(O)OR^2, -(1-4C)alkylN(R^2)C(O)OR^2, -(1-4C)alkylN(R^2)C(O)NR^2R^3, -(1-4C)alkylOC(O)NR^2R^3, (3-6C)cycloalkyl (optionally substituted by 1 or 2 R^8), aryl, heterocyclyl (wherein the heterocyclic ring is linked by a ring carbon atom), -(1-4C)alkylSO_2(2-4C)alkenyl and $-S(O)_cR^2$ (wherein c is 0, 1 or 2);

R^2 and R^3 are independently selected from hydrogen, -O(1-4C)alkyl, -S(1-4C)alkyl, -N(1-4C)alkyl, heterocyclyl, aryl and (1-4C)alkyl [optionally substituted by 1 or 2 R^8 groups]; or

wherein NR^2R^3 may form a 4 to 7 membered saturated, partially saturated or unsaturated ring, optionally containing 1, 2 or 3 additional heteroatoms independently selected from N, O and S (provided there are no O-O, O-S or S-S bonds), wherein any $-CH_2-$ may optionally be replaced by –C(=O)-, and any N or S atom may optionally be oxidised to form an N-oxide or SO or SO_2 group respectively, and wherein the ring is optionally substituted by 1 or 2 substituents independently selected from halo, cyano, (1-4C)alkyl, hydroxy, (1-4C)alkoxy and (1-4C)alkyl$S(O)_b$- (wherein b is 0, 1 or 2);

R^8 is independently selected from hydrogen, hydroxy, (1-4C)alkyl, (2-4C)alkenyl, (1-4C)alkoxy, cyano(1-4C)alkyl, amino(1-4C)alkyl [optionally substituted on nitrogen by 1 or 2 groups selected from (1-4C)alkyl, hydroxy, hydroxy(1-4C)alkyl, dihydroxy(1-4C)alkyl, $-CO_2$(1-4C)alkyl, aryl and aryl(1-4C)alkyl], halo(1-4C)alkyl, dihalo(1-4C)alkyl, trihalo(1-4C)alkyl, hydroxy(1-4C)alkyl, dihydroxy(1-4C)alkyl, (1-4C)alkoxy(1-4C)alkoxy, (1-4C)alkoxy(1-4C)alkyl, hydroxy(1-4C)alkoxy, 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, aryl, heterocyclyl, heterocyclyl(1-4C)alkyl, (3-7C)cycloalkyl (optionally substituted with 1 or 2 hydroxy groups, (1-4C)alkyl or $-CO_2$(1-4C)alkyl), (1-4C)alkanoyl, (1-4C)alkyl$S(O)_b$- (wherein b is 0, 1 or 2), (3-6C)cycloalkyl$S(O)_b$- (wherein b is 0, 1 or 2), aryl$S(O)_b$- (wherein b is 0, 1 or 2), heterocyclyl$S(O)_b$- (wherein b is 0, 1 or 2), benzyl$S(O)_b$- (wherein b is 0, 1 or 2), (1-4C)alkyl$S(O)_c$(1-4C)alkyl- (wherein c is 0, 1 or 2), -N(OH)CHO, $-C(=N-OH)NH_2$, -C(=N-OH)NH(1-4C)alkyl, -C(=N-OH)N((1-4C)alkyl)$_2$, -C(=N-OH)NH(3-6C)cycloalkyl, -C(=N-OH)N((3-6C)cycloalkyl)$_2$, $-COCOOR^9$,

$-C(O)N(R^9)(R^{10})$, $-NHC(O)R^9$, $-C(O)NHSO_2$(1-4C)alkyl, $-NHSO_2R^9$, $(R^9)(R^{10})NSO_2-$, $-COCH_2OR^{11}$, $-COCH_2OH$, $(R^9)(R^{10})N-$, $-COOR^9$, $-CH_2OR^9$, $-CH_2COOR^9$, $-CH_2OCOR^9$, $-CH_2CH(CO_2R^9)OH$, $-CH_2C(O)NR^9R^{10}$, $-(CH_2)_wCH(NR^9R^{10})CO_2R^{9'}$ (wherein w is 1, 2 or 3), and $-(CH_2)_wCH(NR^9R^{10})CO(NR^{9'}R^{10'})$ (wherein w is 1, 2 or 3);
R^9, $R^{9'}$, R^{10} and $R^{10'}$ are independently selected from hydrogen, hydroxy, (1-4C)alkyl (optionally substituted by 1 or 2 R^{11}), (2-4C)alkenyl, (3-7C)cycloalkyl (optionally substituted by 1 or 2 hydroxy groups), cyano(1-4C)alkyl, trihalo(1-4C)alkyl, aryl, heterocyclyl, heterocyclyl(1-4Calkyl), $-CO_2$(1-4C)alkyl; or
R^9 and R^{10} together with the nitrogen to which they are attached, and/or $R^{9'}$ and $R^{10'}$ together with the nitrogen to which they are attached, form a 4- to 6-membered ring where the ring is optionally substituted on carbon by 1 or 2 substituents independently selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl, (1-4C)alkoxy and heterocyclyl; or the ring may be optionally substituted on two adjacent carbons by $-O-CH_2-O-$ to form a cyclic acetal wherein one or both of the hydrogens of the $-O-CH_2-O-$ group may be replaced by a methyl;
R^{11} is independently selected from (1-4C)alkyl, and hydroxy(1-4C)alkyl;
or a pharmaceutically acceptable salt or pro-drug thereof.

2. (original) A compound of the formula (1), or a pharmaceutically acceptable salt or pro-drug thereof, as claimed in claim 1, wherein A is phenylene.

3. (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~or claim 2~~, wherein n is 0.

4 (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~any one of the preceding claims~~ wherein r is 1.

5. (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~any one of the preceding claims~~ wherein m is 1.

6. (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~any one of the preceding claims~~ wherein Y is selected from $-C(O)OR^2$, $-C(O)NR^2R^3$, -(1-4C)alkyl [optionally substituted by a substituent selected from hydroxy, (1-4C)alkoxy, $-S(O)_bR^2$ (wherein b is 0, 1 or 2), $-O-S(O)_bR^2$ (wherein b is 0, 1 or 2), $-NR^2R^3$, $-NR^2C(=O)R^2$ and $-SO_2NR^2R^3$],

-(1-4C)alkylC(O)R^2, -(1-4C)alkylC(O)OR^2, -(1-4C)alkylOC(O)R^2, -(1-4C)alkylC(O)NR^2R^3, -(1-4C)alkylOC(O)OR^2, -(1-4C)alkyl$N(R^2)$C(O)OR^2, -(1-4C)alkyl$N(R^2)$C(O)NR^2R^3, -(1-4C)alkylSC(O)R^2, -(1-4C)alkylOC(O)NR^2R^3, -(1-4C)alkylSO_2(2-4C)alkenyl and -SO_cR^2 (wherein c is 0, 1 or 2).

7. (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~any one of the preceding claims~~ wherein R^2 and R^3 are independently selected from hydrogen, heterocyclyl, -O(1-4C)alkyl, -N(1-4C)alkyl, (1-4C)alkyl [optionally substituted by 1 or 2 R^8 groups]; or an NR^2R^3 group forms a morpholine, thiomorpholine (and oxidised versions thereof), pyrrolidine, or piperidine ring and wherein the ring is optionally substituted by 1 or 2 substituents independently selected from chloro, fluoro, hydroxy and methoxy.

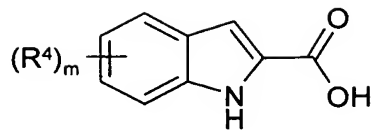
8. (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~any one of the preceding claims~~ wherein R^8 is independently selected from hydrogen, hydroxy, -C(O)N(R^9)(R^{10}), -NHC(O)R^9, -COOR^9, -CH_2OR^9, –CH_2COOR^9, –CH_2OCOR^9, aryl, heterocyclyl, and 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof.

9. (currently amended) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 ~~any one of the preceding claims~~ wherein R^9 and R^{10} are independently selected from hydrogen, hydroxy and (1-4C)alkyl) or R^9 and R^{10} together with the nitrogen to which they are attached form a morpholine, thiomorpholine (and oxidised versions thereof), pyrrolidine, or piperidine ring.

10. (original) A pharmaceutical composition which comprises a compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 in association with a pharmaceutically-acceptable diluent or carrier.

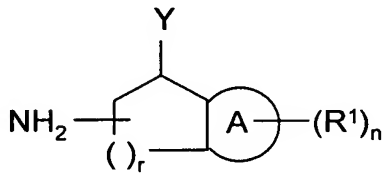
11-15 (cancelled)

16. (original) A process for the preparation of a compound of formula (1) as claimed in claim 1, which process comprises:
reacting an acid of the formula (2):



(2)

or an activated derivative thereof; with an amine of formula (3):



(3)

and thereafter if necessary:

i) converting a compound of the formula (1) into another compound of the formula (1);

ii) removing any protecting groups;

iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.

17. (new) A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 wherein R^4 is selected from chloro, fluoro and methyl.

18. (new) A compound of the formula (I) wherein

A is phenylene;

n is 0;

m is 1;

R^4 is chloro;

Y is selected from $-C(O)OR^2$, $-C(O)NR^2R^3$, -(1-4C)alkyl [optionally substituted by a substituent selected from $-S(O)_bR^2$ (wherein b is 0, 1 or 2), $-O-S(O)_bR^2$ (wherein b is 0, 1 or 2), $-NR^2R^3$, $-NR^2C(=O)R^2$ and $-SO_2NR^2R^3$], -(1-4C)alkylC(O)OR^2, -(1-4C)alkylOC(O)R^2, -(1-4C)alkylC(O)NR^2R^3 , -(1-4C)alkylSC(O)R^2, -(1-4C)alkylSO_2(2-4C)alkenyl and $-SO_cR^2$ (wherein c is 0, 1 or 2);

R^2 and R^3 are independently selected from hydrogen, heterocyclyl, and (1-4C)alkyl [optionally substituted by 1 or 2 R^8 groups]; or an NR^2R^3 group forms a morpholine, thiomorpholine (and oxidised versions thereof), pyrrolidine, or piperidine ring and wherein the ring is optionally substituted by 1 or 2 substituents independently selected from chloro, fluoro, hydroxy and methoxy;

R^8 is independently selected from hydrogen, hydroxy, -C(O)N(R^9)(R^{10}), -NHC(O)R^9, -COOR^9, aryl, heterocyclyl, and 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof;
R^9 and R^{10} are independently selected from hydrogen, hydroxy and (1-4C)alkyl) or R^9 and R^{10} together with the nitrogen to which they are attached form a morpholine ring.

19. (new) A compound of the formula (I) selected from
Methyl (1*R*,2*R*)-2-{[(5-chloro-1*H*-indole-2-yl)carbonyl]amino}indane-1-carboxylate;
5-Chloro-*N*-[(1*R*,2*R*)-1-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]-indole-2-carboxamide;
(1*R*,2*R*)-2-{[(5-chloro-1*H*-indole-2-yl)carbonyl]amino}indane-1-carboxylic acid;
5-Fluoro-*N*-[(1*R*,2*R*)-1-({[(2-hydroxyethyl)amino]sulfonyl}methyl)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide;
N-[(1*R*,2*R*)-1-({[(2-Hydroxyethyl)amino]sulfonyl}methyl)-2,3-dihydro-1*H*-inden-2-yl]-5-methyl-1*H*-indole-2-carboxamide;
N-[(1*R*,2*R*)-1-({[(2-Hydroxyethyl)amino]sulfonyl}methyl)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide;
5-Chloro-*N*-[(1*R*,2*R*)-1-({[(2-hydroxyethyl)amino]sulfonyl}methyl)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide;
5-Fluoro-*N*-((1*R*,2*R*)-1-{[(3-hydroxypropyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;
N-((1*R*,2*R*)-1-{[(3-Hydroxypropyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-5-methyl-1*H*-indole-2-carboxamide;
N-((1*R*,2*R*)-1-{[(3-Hydroxypropyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;
5-Chloro-*N*-((1*R*,2*R*)-1-{[(3-hydroxypropyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;
[((1*R*,2*R*)-2-{[(5-Chloro-1*H*-indol-2-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)thio]acetic acid;
Methyl [((1*R*,2*R*)-2-{[(5-chloro-1*H*-indol-2-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)thio]acetate;
5-Fluoro-*N*-((1*R*,2*R*)-1-{[(2-hydroxyethyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide ;
5-Chloro-*N*-((1*R*,2*R*)-1-{[(2-hydroxyethyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;
N-((1*R*,2*R*)-1-{[(2-Hydroxyethyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-5-methyl-1*H*-indole-2-carboxamide;

N-((1*R*,2*R*)-1-{[(2-Hydroxyethyl)sulfonyl]methyl}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide; and
N-{(1*R*,2*R*)-1-[(2-Amino-2-oxoethyl)thio]-2,3-dihydro-1*H*-inden-2-yl}-5-chloro-1*H*-indole-2-carboxamide.

20. (new) A method of producing a glycogen phosphorylase inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (1) as claimed in claim 1.

21. (new) A method of treating type 2 diabetes, insulin resistance, syndrome X, hyperinsulinaemia, hyperglucagonaemia, cardiac ischaemia or obesity in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (1) as claimed in claim 1.

22. (new) A method of treating type 2 diabetes in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (1) as claimed in claim 1.